

The embodiments of the invention in which an exclusive property or privilege is claimed are defined as follows:

1. A method of preemptively inhibiting pain and inflammation at a wound during a surgical procedure, comprising delivering to a wound during a surgical procedure a solution comprising at least one pharmacological agent selected from the group consisting of a mitogen-activated protein kinase (MAPK) inhibitor, an α_2 -receptor agonist, a neuronal nicotinic acetylcholine receptor agonist, a cyclooxygenase-2 (COX-2) inhibitor, a soluble receptor and mixtures thereof, wherein the solution is applied locally and perioperatively to the surgical site.

2. The method of Claim 1, wherein the pharmacological agent is a MAPK inhibitor selected from the group consisting of 4-(4-fluorophenyl)-2-(4-methylsulfinylphenyl)-5-(4-pyridyl)-1H-imidazole, [4-(3-iodophenyl)-2-(4-methylsulfinylphenyl)-5-(4-pyridyl)-1H-imidazole], [4-(4-fluorophenyl)-2-(4-hydroxyphenyl)-5-(4-pyridyl)-1H-imidazole], [4-(4-fluorophenyl)-2-(4-nitrophenyl)-5-(4-pyridyl)-1H-imidazole], and 2'-Amino-3'-methoxyflavone.

3. The method of Claim 1, wherein the pharmacological agent is an α_2 -receptor agonist selected from the group consisting of clonidine; dexmedetomidine; oxymetazoline; (R)-(-)-3'-(2-amino-1-hydroxyethyl)-4'-fluoro-methanesulfoanilide (NS-49); 2-[(5-methylbenz-1-ox-4-azin-6-yl)imino]imidazoline (AGN-193080); AGN 191103; AGN 192172; 5-bromo-N-(4,5-dihydro-1H-imidazol-2-yl)-6-quinoxalinamine (UK14304); 5,6,7,8-tetrahydro-6-(2-propenyl)-4H-thiazolo[4,5-d]azepin-2-amine (BHT920); 6-ethyl-5,6,7,8-tetrahydro-4H-oxaazolo[4,5-d]azepin-2-amine (BHT933); and 5,6-dihydroxy-1,2,3,4-tetrahydro-1-naphyl-imidazoline (A-54741).

4. The method of Claim 1, wherein the pharmacological agent is a neuronal nicotinic acetylcholine receptor agonist selected from the group consisting of (R)-5-(2-azetidylmethoxy)-2-chloropyridine (ABT-594); (S)-5-(2-azetidylmethoxy)-2-chloropyridine (S-enantiomer of ABT-594); 2-methyl-3-(2-(S)-pyrrolidinylmethoxy)pyridine (ABT-089); (R)-5-(2-Azetidinylmethoxy)-2-chloropyridine (ABT-594); (2,4)-Dimethoxy-benzylidene anabaseine (GTS-21); SBI-1765F; RJR-2403; 3-((1-methyl-2(S)-pyrrolidinyl)methoxy)pyridine (A-84543); 3-(2(S)-azetidylmethoxy)pyridine (A-85380); (+)-anatoxin-A and (-)-anatoxin-A (1R)-

1-(9-Azabicyclo[4.2.2]non-2-en-2-yl)-ethanoate fumarate, and (R,S)-3-pyridyl-1-methyl-2-(3-pyridyl)azetidine (MPA).

5. The method of Claim 1, wherein the pharmacological agent is a COX-2 inhibitor selected from the group consisting of celecoxib, meloxicam, nimesulide, nimesulide, diclofenac, flosulide, N-[2-(cyclohexyloxy)-4-nitrophenyl]-methanesulfonamide, 1-[(4-methylsulfonyl)phenyl]-3-trifluoromethyl-5-[(4-fluoro)-phenyl]pyrazole, DuP 697, SC-58451, RS-57067, SC-57666 and L-745,337.

6. The method of Claim 1, wherein the pharmacological agent is a soluble receptor selected from the group consisting of tumor necrosis factor (TNF) soluble receptors, interleukin-1 (IL-1) cytokine receptors, class I cytokine receptors, and receptor tyrosine kinases.

7. The method of Claim 1, wherein the solution further comprises at least one additional pain/inflammation inhibitory agent selected to act on a different molecular target than the pharmacological agent.

8. The method of Claim 1, comprising continuously applying the solution to the wound.

9. The method of Claim 8, comprising continuously irrigating the wound with the solution.

10. The method of Claim 1, wherein the solution is applied by irrigation of the wound.

11. The method of Claim 1, wherein the perioperative application of the solution comprises intraprocedural application together with preprocedural or postprocedural application of the solution.

12. The method of Claim 1, wherein the perioperative application of the solution comprises preprocedural, intraprocedural and postprocedural application of the solution.

13. The method of Claim 1, wherein each of the pharmacological agent in the solution is delivered locally at a concentration of no greater than 100,000 nanomolar.

14. The method of Claim 7, wherein the at least one additional pain/inflammation inhibitory agent is selected from the group consisting of: serotonin receptor antagonists; serotonin receptor agonists; histamine receptor antagonists; bradykinin receptor antagonists; kallikrein inhibitors; tachykinin receptor antagonists including neurokinin₁ receptor subtype antagonists and neurokinin₂ receptor subtype antagonists; calcitonin gene-related peptide receptor antagonists; interleukin receptor antagonists; phospholipase inhibitors including PLA₂ isoform inhibitors and PLC_γ isoform inhibitors; cyclooxygenase inhibitors; lipooxygenase inhibitors; prostanoid receptor antagonists including eicosanoid EP-1 receptor subtype antagonists and eicosanoid EP-4 receptor subtype antagonists and thromboxane receptor subtype antagonists; leukotriene receptor antagonists including leukotriene B₄ receptor subtype antagonists and leukotriene D₄ receptor subtype antagonists; opioid receptor agonists including μ-opioid receptor subtype agonists, δ-opioid receptor subtype agonists, and κ-opioid receptor subtype agonists; purinoceptor agonists and antagonists including P_{2Y} receptor agonists and P_{2X} receptor antagonists; and ATP-sensitive potassium channel openers.

15. A solution for use in the preemptive inhibition of pain and inflammation at a wound during a surgical procedure, comprising at least one pharmacological agent selected from the group consisting of a mitogen-activated protein kinase (MAPK) inhibitor, an α₂-receptor agonist, a neuronal nicotinic acetylcholine receptor agonist, a cyclooxygenase-2 (COX-2) inhibitor, a soluble receptor and mixtures thereof, in a liquid carrier, the concentration of said pharmacological agent within the solution being the concentration of that agent which is desired to be delivered locally, in the absence of metabolic transformation, to a wound in order to achieve a predetermined level of inhibitory effect at the wound.

16. The solution of Claim 16, wherein the pharmacological agent is selected from the group consisting of 4-(4-fluorophenyl)-2-(4-methylsulfinylphenyl)-5-(4-pyridyl)-1H-imidazole, [4-(3-iodophenyl)-2-(4-methylsulfinylphenyl)-5-(4-pyridyl)-1H-imidazole], [4-(4-fluorophenyl)-2-(4-hydroxyphenyl)-5-(4-pyridyl)-1H-imidazole], [4-(4-fluorophenyl)-2-(4-nitrophenyl)-5-(4-pyridyl)-1H-imidazole], 2'-Amino-3'-methoxyflavone, clonidine; dexmedetomidine; oxymetazoline; (R)-(-)-3'-(2-amino-1-hydroxyethyl)-4'-fluoro-methanesulfoanilide (NS-49); 2-[(5-methylbenz-1-ox-4-azin-6-yl)imino]imidazoline (AGN-193080); AGN 191103; AGN 192172; 5-bromo-N-(4,5-dihydro-1H-imidazol-2-yl)-6-quinoxalinamine (UK14304); 5,6,7,8-

tetrahydro-6-(2-propenyl)-4H-thiazolo[4,5-d]azepin-2-amine (BHT920); 6-ethyl-5,6,7,8-tetrahydro-4H-oxaazolo[4,5-d]azepin-2-amine (BHT933); 5,6-dihydroxy-1,2,3,4-tetrahydro-1-naphyl-imidazoline (A-54741), (R)-5-(2-azetidinylmethoxy)-2-chloropyridine (ABT-594); (S)-5-(2-azetidinylmethoxy)-2-chloropyridine (S-enantiomer of ABT-594); 2-methyl-3-(2-(S)-pyrrolidinylmethoxy)pyridine (ABT-089); (R)-5-(2-Azetidinylmethoxy)-2-chloropyridine (ABT-594); (2,4)-Dimethoxybenzylidene anabaseine (GTS-21); SBI-1765F; RJR-2403; 3-((1-methyl-2(S)-pyrrolidinyl)methoxy)pyridine (A-84543); 3-(2(S)-azetidinylmethoxy)pyridine (A-85380); (+)-anatoxin-A and (-)anatoxin-A (1R)-1-(9-Azabicyclo[4.2.2]non-2-en-2-yl)-ethanoate fumarate, (R,S)-3-pyridyl-1-methyl-2-(3-pyridyl)azetidine (MPA), celecoxib, meloxicam, nimesulide, nimesulide, diclofenac, flosulide, N-[2-(cyclohexyloxy)-4-nitrophenyl]-methanesulfonamide, 1-[(4-methylsulfonyl)phenyl]-3-trifluoromethyl-5-[(4-fluoro)phenyl]pyrazole, DuP 697, SC-58451, RS-57067, SC-57666, L-745,337, tumor necrosis factor (TNF) soluble receptors, interleukin-1 (IL-1) cytokine receptors, class I cytokine receptors, receptor tyrosine kinases and mixtures thereof.

17. The solution of Claim 15, which further comprises at least one additional pain/inflammation inhibitory agent selected to act on a different molecular target than the at least one pharmacological agent.

18. The solution of Claim 17, wherein the pharmacological agent and each of the additional pain/inflammation inhibitory agents in the solution is included at a concentration of no greater than 100,000 nanomolar, adjusted for dilution in the absence of metabolic transformation, at an intended local delivery site.

19. The solution of Claim 17, wherein the at least one additional pain/inflammation inhibitory agents are selected from the group consisting of: serotonin receptor antagonists; serotonin receptor agonists; histamine receptor antagonists; bradykinin receptor antagonists; kallikrein inhibitors; tachykinin receptor antagonists including neurokinin₁ receptor subtype antagonists and neurokinin₂ receptor subtype antagonists; calcitonin gene-related peptide receptor antagonists; interleukin receptor antagonists; phospholipase inhibitors including PLA₂ isoform inhibitors and PLC_γ isoform inhibitors; cyclooxygenase inhibitors; lipooxygenase inhibitors; prostanoid receptor antagonists including eicosanoid EP-1 receptor subtype antagonists and eicosanoid EP-4 receptor subtype antagonists and thromboxane receptor subtype antagonists; leukotriene receptor antagonists including leukotriene

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